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Application Number

09/471 349

Filed

Aug 27, 2001

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(12) **United States Patent**  
**Sahni et al.**

(10) Patent No.: **US 7,163,817 B2**  
(45) Date of Patent: **Jan. 16, 2007**

(54) **CLOT-SPECIFIC STREPTOKINASE  
PROTEINS POSSESSING ALTERED  
PLASMINOGEN ACTIVATION  
CHARACTERISTICS AND A PROCESS FOR  
THEIR PREPARATION**

5,434,073 A \* 7/1995 Dawson et al. .... 435/216  
5,772,996 A \* 6/1998 Atkinson ..... 424/94.4  
6,054,312 A \* 4/2000 Larocca et al. .... 435/320.1

**FOREIGN PATENT DOCUMENTS**

EP 0 397 366 11/1990  
WO WO 91/17765 11/1991

**OTHER PUBLICATIONS**

Wishart et al, A single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. *J Biol Chem.* Nov. 10, 1995;270(45):26782-5.\*  
Witkowski et al, Conversion of a beta-ketoacyl synthase to a malonyl decarboxylase by replacement of the active-site cysteine with glutamine. *Biochemistry.* Sep. 7, 1999;38(36):11643-50.\*  
Goldstein et al, A chimeric streptokinase with unexpected fibrinolytic selectivity. *Thromb Haemost.* Sep. 1996;76(3):429-38.\*  
EMBL database ID No. HSFIBI Jul. 16, 1988 Gronostajski et al.\*  
U.S. Appl. No. 10/631,588 Sahni et al, filed Jul. 31, 2003. STIC in house alignment of SEQ ID No.: 2 and SEQ ID No.: 11.\*  
Kornblitt et al., Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene. *EMBO J.* Jul. 1985;4(7):1755-9.\*  
Banerjee et al, Streptokinase—a clinically useful thrombolytic agent. *Biotechnol Adv.* Feb. 2004;22(4):287-307. Review.\*  
Jackson et al, Active streptokinase from the cloned gene in *Streptococcus sanguis* is without the carboxy-terminal 32 residues. *Biochemistry.* Jan. 14, 1986;25(1):108-14.\*  
Johnson et al, Influence of primary sequence transpositions on the folding pathways of ribonuclease T1. *Biochemistry.* Aug. 6, 1996;35(31):10223-33.\*  
Galys et al, Identification of regions in interleukin-1 alpha important for activity. *FEBS J.* Oct. 15, 1993;268(29):22105-11.\*  
Whistock et al, Prediction of protein function from protein sequence and structure. *FEBS Rev Biophys.* Aug. 2003;36(3):307-40. Review.\*  
Lucas et al., The binding of human plasminogen to fibrin and fibrinogen. *J Biol Chem.* Apr. 10, 1983;258(7):4249-56.\*  
Williams et al., Solution structure of a pair of fibronectin type I modules with fibrin binding activity. *J Mol Biol.* Jan. 28, 1994;235(4):1302-11.\*  
Huston et al., Protein engineering of antibody binding sites: recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in *Escherichia coli*. *Proc Natl Acad Sci U S A.* Aug. 1988;85(16):5879-83.\*

(Continued)

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(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/940,235**

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(30) **Foreign Application Priority Data**

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**C12N 9/48** (2006.01)  
**C12P 21/00** (2006.01)  
**C12P 21/06** (2006.01)

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435/69.7; 435/70.1; 435/71.1

(58) Field of Classification Search ..... 435/216,  
435/183  
See application file for complete search history.

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

5,026,772 A \* 6/1991 Kobayashi et al. .... 525/54.1  
5,151,412 A \* 9/1992 Brown ..... 514/8  
5,187,098 A 2/1993 Malke et al. .... 435/320.1

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(57) **ABSTRACT**

The invention disclosed herein provides clot specific streptokinase proteins possessing altered plasminogen characteristics, including enhanced fibrin selectivity. The kinetics of plasminogen activation by these proteins are distinct from those of natural streptokinase, in that there is a temporary delay or lag in the initial rate of catalytic conversion of plasminogen to plasmin. Also disclosed are processes for preparing the proteins.

**3 Claims, 26 Drawing Sheets**